Aseptic meningitis caused by Coronavirus OC43

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### Abstract

Human coronavirus OC43 (HCoV-OC43) is one of the coronaviruses that cause the mild cold. On the other hand, extra-respiratory manifestations such as central nervous system infections with HCoV-OC43 are very rarely reported. We present a case of a previously healthy immunocompetent child with acute aseptic meningitis, as a result of HCoV-OC43 who admitted to the emergency department with a complaint of unconsciousness.. Respiratory tract and cerebrospinal fluid culture showed HCoV-OC43 in viral screening. During the follow-up period, the patient was completely asymptomatic, with normalized consciousness. The clinicians should keep in mind that HCoV-OC43 can be the etiological agent in the differential diagnosis of aseptic meningitis in immunocompetent individuals with reversible neurological symptoms.

## Keywords

Aseptic Meningitis, Cerebrospinal Fluid, Children, Human Coronavirus, HCoV-OC43

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# Introduction

Central nervous system (CNS) infections are categorized as meningitis and encephalitis [1]. Aseptic meningitis, with negative bacterial and fungal cultures is the most common form of meningitis. Acute onset of meningeal irritation signs and cerebrospinal fluid (CSF) pleocytosis; (CSF) under microscopy (40x) shows more than 5 white blood cells/mm3) [2]. The viral etiology of the majority of aseptic meningitis cases is unknown. However, the development in PCR technology provided us to diagnose viral microorganisms [3]. Human coronaviruses (HCoVs) OC43 are associated most frequently with upper respiratory tract infection and less frequently with lower respiratory tract infections, including bronchiolitis, croup, and pneumonia, primarily in infants and especially in immunocompromised children. On the other way, extrarespiratory manifestations such as CNS infections with HCoV-OC43 have been reported very rarely. Herein we report a case of a previously healthy immunocompetent 2-year-old male with acute aseptic meningitis, as a result of HCoV-OC43

# Case Report

A 2-year-old male presented unconsciousness with no exacerbating or relieving factors. There were no additional complaints suggesting infection such as fever, runny nose, cough, malaise, diarrhea, and vomiting. His brother had been coughing for 4 days who was also autistic. His weight was 11 kg (3-10 percentile). His blood pressure was 90/60 mm Hg. He had a heart rate of 100 beats/min, body temperature of less than 36.5°C, and SpO2 of 98% on room air. No skin rash was reported. He had a tendency to sleep and was restless. His pediatric coma scale was 9. The rest of his full neurological assessment was within normal limits. During the follow up period neck stiffness and a positive Kernig's sign was elicited



**Table 1.** Axial CT image: Mild enlargement of the extracerebral

 CSF space is observed in the bilateral frontal area

in two hours. He had normal papillary reflexes and no sign of bilateral papilledema. His body temperature became 37.8°C. His blood tests revealed normal renal, liver biochemistry and venous blood gas analysis. The full blood count revealed a white blood cell count of 6240 µL (neutrophils: 49%, lymphocytes: 44%, monocytes 5%, eosinophils 2%), hemoglobin 10.2 g/ dL and thrombocyte count of 429.000/mm3. The CRP was 6.08 mg/L (N<5). Lumbar puncture (LP) was made for clinical diagnosis of meningitis. No microorganisms were isolated in (CSF). His contrast-enhanced computed tomography showed mild enlargement of the extracerebral CSF space in the bilateral frontal area (Figure 1). The CSF examination showed no white cell count, but 10 erythrocytes /mm3. The CSF glucose level was 50 mg/dl (simultaneous blood glucose was 74 mg/dl) and the protein level was 15 mg/dl. Herpes PCR, Herpes type 1-2 IgM, Herpes type 1-2 IgG serologies sent from the CSF were negative. CSF culture for bacteria was also negative. Due to the COVID-19 pandemic, we searched also COVID-19 PCR, which was negative. Interestingly respiratory viral screening showed HCoV-OC43. Therefore, CSF was also searched for HCoV-OC43 PCR that was found positive. The quantitative immunoglobulin levels (Ig G, M, A) were in the normal range. During the follow-up period the patient was recovered, with normalized consciousness.

# Discussion

This was a case of aseptic meningitis due to HCoV-OC43 in a healthy child with central nervous system symptoms. According to our knowledge, there are very rare reports of meningitis secondary to HCoV-OC43 among immunocompetent pediatric patients.

Meningitis is an acute inflammation of the meninges. The presenting symptoms of meningitis are headache, fever, vomiting, neck stiffness and sometimes consciousness [4]. The diagnostic tests currently used to detect viral microorganisms that cause CNS infections are multiplex PCR assay and metagenomic next-generation sequencing (mNGS) [5]. Thus, we detected HCoV-OC43 using multiplex PCR assay. The unknown causes were probably due to the limitations of laboratory testing, such as the limitation of PCR panel testing. Meningitis of unknown cause was reported in 81.5% in the USA, and 42% in the UK [6].

Following the SARS global outbreak, some clinical laboratories started offering comprehensive respiratory molecular diagnostic testing using reverse transcriptase-polymerase chain reaction (RT-PCR) assays, some of which include HCoVs 229E, OC43, NL54, and HKU1 as targets. Thus, we diagnosed the microorganism, otherwise it could have been skipped.

Coronaviridae are the largest enveloped RNA viruses with a positive single-stranded RNA molecule [7]. HCoV-OC43 belongs to the Betacoronavirus genus like SARS-CoV-2 [8]. Multiplex PCR for CSF was positive for HCoV-OC43, which led to the final diagnosis. It was considered reasonable to assume that the infection had been caused by HCoV-OC43 after the detection in the nasopharyngeal swab fluid.

# Conclusion

This case demonstrates that HCoVs-OC43 may be considered in differential diagnosis of aseptic meningitis in immunecompetent individuals with reversible neu-rological symptoms.

### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

# Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

# **Conflict of interest**

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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